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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,738	05/24/2000	MICHAEL BLATT	2186PB-1	2749

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EXAMINER
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ART UNIT	PAPER NUMBER
1653	23

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,738	BLATT ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Paper #22, filed February 20, 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10 and 57-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10 and 57-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

This Office Action is in response to Paper #22, filed February 20, 2003. Claims 3 and 21-56 have been canceled. Claim 1, 2, 4-20, and 57-65 are currently pending and are under examination.

Priority is set to September 30, 1997.

Withdrawal of Objections and Rejections

The objection to the specification and claims for sequence identification informalities is withdrawn.

The objection to the specification for lack of cross-reference of priority applications is withdrawn.

The objection to the specification because it contains an embedded hyperlink and/or other form of browser-executable code is withdrawn.

This application has been filed with informal drawings which are acceptable for examination purposes only. Applicants state that formal drawings will be submitted upon allowance. However, **the drawings comprise the draftsman's stamp and are now considered formal.**

The objection to Claim 3 under 37 CFR 1.75 is withdrawn.

The rejection of the Claims under 35 U.S.C. 101 is withdrawn.

The rejection of the Claims under 35 U.S.C. 112, first paragraph, for scope of enablement as set forth in the previous Office Action is withdrawn.

The rejection of the Claims under 35 U.S.C. 112, first paragraph, for lack of written description as set forth in the previous Office Action is withdrawn.

The rejection of the Claims under 35 U.S.C. 112, second paragraph, as set forth in the previous Office Action is withdrawn.

The rejection of the Claims under 35 U.S.C. 102(b) as being anticiapted by Leung et al. (1994; Science 264:1448-1452) is withdrawn.

The rejection of Claims 1, 17, 20, and 26 under 35 U.S.C. 102(b) as being anticipated by Silhavy et al. (1995; Plant Molecular Biology 27:587-595) is withdrawn.

New Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-20 and 57-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Reference to SEQ ID NO: 4 has now been added to the claims, though it does appear that such was intended by reference to the nucleotide sequence SEQ ID NO: 3, which encodes SEQ ID NO: 4, in Claim 18. However, without the reference, SEQ ID NO: 4 could not be examined in the last office action.

At page 42, the last sentence of paragraph 1, states that "However, unlike other syntaxin proteins characterised to date, Nt-Syr (which is SEQ ID NO: 2) was found to include a single, EF-hand consensus sequence (SEQ ID NO: 33) between amino acids residues 16 and 28, and a putative nucleotide binding site (SEQ ID NO: 34) between residues 14 and 19".

The Examiner has found the nucleotide binding sequence (NBS) of SEQ ID NO: 2 in SEQ ID NO: 4. NBS is amino acids 114-119 of SEQ ID NO: 2 and amino acids 124-129 of SEQ ID NO: 4 which is: G C G P G S

The Examiner has found a believable coiled coil region having an epimorphin pattern in SEQ ID NO: 4 when compared to SEQ ID NO: 2 with an eye towards FIG. 10, as evidenced below:

Coiled coil is amino acids 210-247 of SEQ ID NO: 2

R H E A V K E **L E** R **N** L K **E L H** Q V **F** L **D M A** V **L V E S Q G** A Q L **D** D **I E** S

Coiled coil is amino acids 220-257 of SEQ ID NO: 4

R H D R V K D **I E** K N L R **E L H** Q V **F** L **D M A** V **L V E** H **Q G** A Q L **D** D **I E** S

The Examiner has found the hydrophobic C-terminal of SEQ ID NO: 4. The hydrophobic C is amino acids 282-296 of SEQ ID NO: 2 and of SEQ ID NO: 4 and is: N T **R** K W T C **I** A **I I** I L I I

The Examine has not found the EF-hand consensus sequence in SEQ ID NO: 4. The EF – hand consensus sequence is 16-28 of SEQ ID NO: 2: N Q S D S H A I E M G D I, and this sequence or even similar sequence is not found in SEQ ID NO: 4.

Therefore, if those regions that define the instant proteins over the prior art syntaxins that are found in SEQ ID NO: 2 are not found in SEQ ID NO: 4, and SEQ ID NO: 4 has not been shown in the specification to have the ability to affect or inhibit ABA mediated control of ions channels like SEQ ID NO: 2 has, then it cannot be concluded that SEQ ID NO: 4 has this ability because it lacks a defining structural characteristic of a protein having this ability. The Examiner is not questioning that the protein described as SEQ ID NO: 4 may be a member of the syntaxin family; rather, the question is, without the defining EF-hand consensus sequence which provides evidence that a syntaxin family member has the ability to affect or inhibit ABS mediated control of ions channels, this function cannot be predictably assigned this protein having SEQ ID NO: 4. Indeed, it is this EF-hand consensus sequence that was suggested by Leung et al. to provide evidence that the ABI1 gene product integrates ABA and calcium ion signals. Therefore, the necessity of the EF-hand consensus sequence for altering ABA ion channel function is supported by the prior art.

In *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary: The specification teaches how to determine if proteins, and in particular syntaxin family proteins, have the ability to inhibit ABA mediated control of ion channels via that protein described as SEQ ID NO: 2. As noted above, Nt-Syr (which is SEQ ID NO: 2) was found to include a single, EF-hand consensus sequence between amino acids residues 16 and 28, and a putative nucleotide binding site between residues 14 and 19 and these structural features lend itself to having the ability to inhibit ABA meditated control of ion channels. Therefore, one skilled in the art would have to determine for themselves what the function of the protein described as SEQ ID NO: 4 does.

2) Amount of direction or guidance presented: Direction and guidance is provided in an overall sense – see the strategy set forth on page 19+.

3) Presence or absence of working examples: There are working examples, which the protein having SEQ ID NO: 2 is found to be responsive to ABA.

4) Nature of the invention; 5) State of the prior art; 6) Relative skill of those in the art: The nature of the invention is complex and the prior art recognizes proteins that are responsive to ABA. Those working in the art are highly skilled.

7) Predictability or unpredictability of the art: It is not predictable which proteins will be involved in ABA signaling, including those proteins have augmented levels in response to ABA.

8) Breadth of the claims: The breadth of these claims are not particularly broad.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

Claims 1, 2, 13-18, 20, 57-60, 64 and 65 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims lack written description in the specification because there is no correlation of structure and function. Specifically, the specification does not describe proteins that increase or augment the ABA mediated control of ion channels. Regarding Claims 1, 2, and 13-18. The specification does not teach the protein described in Claim 1, for example, that will augment ABA mediated control of ion channels. How will this protein differ from a protein that inhibits or attenuates the ABA mediated control of ion channels. Such is not described in the specification.

The specification does not describe variants of SEQ ID NO: 2 or NO: 4, for example, to include those having per cent homology to these sequences, that have the ability to increase ABA mediated control of ion channels.

Claim 17 continues to lack written description for the same reason as set forth in the previous Office Action, that is, the speicifcation doesn ot teach a mammalian protein responsive to ABA.

Therefore, the claims lack written description.

Regarding Claim 17, Applicants point out that mammalian homologues of syntaxin protein have been identified. The Examiner agrees. But *ABA is a plant phytohormone*. Therefore, how can an mammalian syntaxin homologue of NtSyr be responsive to ABA? Such is not described.

While the rejection has changed with the amendments to the claims, Applicants have urged that the addition of functional language has been presented and therefore the claims have written description. Only one parameter of that function is described; the other end of the function lacks written description.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 19 presents new matter. While Applicants point to the specification at pages 5-6 to provide basis for the amendment to Claim 19, this passage refers to two hybrid systems involving fusion proteins and recombinant technology. As written, Claim 19 appears to be directed to a binding assay between two proteins, and this is not set forth in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-20, 64, and 65 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 refers to variants. As broad as the structural language is, it appears that variants are redundant. If not, it is not clear what a variant of a structure is.

In Claim 19, it is not clear how the interaction of the proteins is determined. It is not clear how the method is "isolated".

In Claim 20, it is not clear which protein is selected.

Upon perusal of the claims, the following concerns should have been raised in the previous Office Action. That is, Claim 5 broadens Claim 4 by reciting a smaller fragment within amino acids 282-296 of SEQ ID NO: 2. The same has been done in Claim 7 and Claim 9. In Claim 11, there is no antecedent basis to specify specific amino acids, and certainly not to specific amino acids number 120 which lies outside of the NBS specified as 114-199 of SEQ ID NO: 2.

Claims 1, 17, 20 are rejected under 35 U.S.C. 102(b) as being anticiapted by Leung et al. (1994; Science 264:1448-1452). Leung et al. teach *Arabidopsis* ABA response gene product ABI1, which is a calcium-modulated protein phosphatase. This phosphatase comprises and EF hand consensus sequence as shown in Fig. 4. Further, Leung et al teach that the stomatal opening as well as some of the electrogenic units involved (such as plasma membrante H pump and inward rectifying K channels) are sensitive to protein phosphorylation (page 1451). Therefore, Leung et al. teach a protein comprising a biologically active fragment or variant of the protein of Claim 1

which is capable of affecting ABA mediated control of ion channels (Claim 1) from plants (Claim 17). Leung et al. also teach that Abl1 may interact with $p34^{cdc2}$ (page 1450, col. 2, para. 2). Thus, $p34^{cdc2}$ anticipates Claim 20.

Applicants urge that the structural protein described in Claim 1 is not found in Leung et al. The Examiner agrees. However, a protein comprising a biologically active fragment or variant as set forth in the amendment to the claims which affects ABA function is. Therefore, teachings of Leung et al. have been modified.

No Claims are Allowed.

It appears that if Claim 1 were amended to recite the following it would be allowable:

An isolated protein comprising:

(i) a hydrophobic C-terminus;

(ii) at least one coiled coil region;

(iii) an EF-hand consensus sequence;

(iv) a nucleotide binding site; and optionally

(v) a hydrophilic N-terminus;

wherein said protein inhibits absicisic acid (ABA) mediated control of ion channels.

Of course, other amendments to the claims would have to take place to overcome all of the rejections above.

This is a very broad claim. However, the structural descriptions are known in the art. These structural regions are pointed out in the specification and demonstrated across proteins as

shown in Figure 10. The combination of the structures have not been found in the prior art. Further, the elicited activity for this structure is not found. The claim is enabled. Hopefully, this draft claim will provide Applicants with a clear demonstration of amendments to the claims that would over come the rejections made herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 703-308-0034. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 703-308-2329. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER